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EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	18

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/841,720	YU, LEI	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-24,26-32 and 34-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-24,26-32 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A-C* .

DETAILED ACTION

1. Formal Matters

A. Amendment C, filed 7/31/03, has been entered into the record.

B. The Information Disclosure Statement, filed 6/6/01, has been entered into the record.

C. Claims 1-18 were pending. In Preliminary Amendment AA, Applicants canceled claims 1-17 and added new claims 18-37. However, it appears that Applicants intended claim 18 to also be canceled since they requested the entry of new claim 18. Therefore, claims 18-36 have been renumbered under 37 CFR 1.126 as claims 19-37. Therefore, claims 19-37 are pending and were subject to restriction in Paper No. 15, dated 5/27/03. In Amendment C, Applicants canceled claims 24 and 32 (new claims 25 and 33, respectively) and elected Group I as drawn to SEQ ID NO:1. Therefore, claims 19-24, 26-32 and 34-37 are the subject of this Office Action. The Examiner requests verification of this action.

2. Title

A. The title is objected to since the syntax could be improved by amending the title to recite, for example, "Methods of using mu opioid receptors."

3. Figures

A. The specification is objected to since Figure 1 would be clearer, since it appears that Figure 1B is merely a continuation of Figure 1A, that the Figures be relabeled as "Figure 1" and "Figure 1 continued," especially in view of the fact that the specification does not distinguish "1A" and "1B." If Applicants wish to keep the Figures listed as "1A" and "1B" then the Brief Description of the Figures should be amended to reflect this.

4. Claim Objections

A. Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of previous claim 23. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 23 and 24 recite the same process step using SEQ ID NO:1.

B. Claims 23, 24, 32 are objected to since they depend from rejected base claims, as seen in the rejections below under 35 USC 112, first paragraph.

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 19-22, 26-31 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of screening compounds for their ability to bind the opioid receptor of SEQ ID NO:1, does not reasonably provide enablement for methods of screening compounds for their ability to bind fragments of opioid receptors which are less than the full-length of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth is excessive with regard to Applicants claiming methods for screening candidate substances which bind to opioid receptors using any receptor fragment less than the full-length encoded by SEQ ID NO:1. First, it is believed, but cannot be confirmed, that the opioid receptor seen in the Figures and used in the Examples is that of SEQ ID NO:2. It is suggested that Applicants point out exactly where in the specification the use of SEQ ID NO:2 is shown. Furthermore, even if SEQ ID NO:2 was used, Applicants would only be enabled for the use of this receptor. The claims recite using fragments of this receptor comprising as few as 25 nucleotides of SEQ ID NO:1. Applicants have provided no guidance or working examples of any functional opioid receptor less than the full-length of SEQ ID NO:1. The claims recite providing or expressing a recombinant opioid receptor comprising at least 25 bases of SEQ ID NO:1. Applicants have not only not taught which domains are responsible for ligand binding and receptor function, but they have not taught what amino acids would define an opioid receptor. In other words, according to the claims, an opioid receptor can be as few as 25 bases of SEQ ID NO:1 (8 amino acids). Opioid receptors are hundreds of amino acids in length. Therefore, Applicants are

not only claiming every opioid receptor comprising at least 25 bases of SEQ ID NO:1, but the claims do not even require that binding or functional domains be included. Furthermore, it is not predictable to the artisan how to make a functional opioid receptor which is as few as 8 amino acids of SEQ ID NO:1

Therefore, in summary, the breadth of the claims is excessive with regard to Applicants claiming methods using any and all opioid receptors other than the full length of SEQ ID NO:1. Applicants have not provided any guidance or working examples of structural, binding, or functional domains which make up opioid receptors, nor would it be predictable to the artisan how to make a functional opioid receptor other than that of the full-length of SEQ ID NO:1. For these reasons, the Examiner has concluded that undue experimentation would be required to practice the invention as claimed.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 19-22, 26-31 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Methods of using opioid receptors other than that encoded by SEQ ID NO:1 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotide and would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:2.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1 and 2 alone are insufficient to describe the genus.

The specification provides a written description of only a small number of these nucleic acid constructs (SEQ ID NO:1). No other species are described, or structurally contemplated, within the

instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical nucleic acid residues which would structurally characterize the genus of nucleic acids encoding the genus of opioid proteins claimed, because it is unknown and not described what structurally constitutes any different nucleic acids encoding an opioid receptor, or nucleic acids encoding opioid receptors from any different species, which are further not described; thereby not meeting the written description requirement under 35 USC 112, first paragraph. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

7. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 26 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what the metes and bounds of part (i) of the claim is regarding "binding ability" especially in view of part (ii), which also recites binding ability.

Furthermore, regarding claim 26, parts (iii) and (iv) are confusing since these are functional assays and do not necessarily demonstrate that the candidate substances bind to the polypeptide, only that they have a functional effect, especially in light of the fact that the ion channels are not even required to be modulated by the opioid receptor. The claim implies that an effect on any ion channel would demonstrate that the compound binds the opioid receptor.

Similarly, regarding claim 36, parts (i) and (ii) are confusing since these are binding assays and do not necessarily demonstrate that the candidate substances are either agonists, or antagonists – i.e. no functional assay is required.

B. Claims 28-32 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: one which differentiates the claims from claims 19-24, 26 and 27. It appears that the only difference between these sets of claims is the use of the term "expressing" in claim 28 vs. "providing." This implies that claim 19 does not require a cell, but that claim 28 does. Therefore, claim 28 should be amended to incorporate transfection of the DNA into a cell.

C. Claims 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: one which is able to differentiate agonists from antagonists (i.e. specific results in an opioid assay).

D. Claims 35-37 are further confusing since it is not understood how the artisan can determine whether or not a compound is an agonist or antagonist simply by measuring its ability to bind a receptor. No functional assays are provided in the claims to be able to identify agonists and antagonist.

8. Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

A. Claims 19-24, 26-32 and 34-36 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of one or more claims of copending Application No. 09/626,616. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. This application was not available to the Examiner at the time of this Office Action. However, it was noticed that both applications are drawn to methods of screening opioid compounds.

9. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 19-22, 26, 28-31, 35 and 36 are rejected under 35 U.S.C. 102(a) as being anticipated by Evans et al. (U.S. Patent No. 6,265,563). The claims recite methods of screening candidate substances for their ability to bind an opioid receptor comprising at least 25 contiguous bases of SEQ ID NO:1, or which comprises SEQ ID NO:2. Chen et al. meet these limitations (Sequence Comparisons A and C; "Abstract" and page 9 under "binding analysis").

B. Claims 19-22, 26 and 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Evans et al. (U.S. Patent No. 6,265,563). The claims recite methods of screening candidate substances for their ability to bind an opioid receptor comprising at least 25 contiguous bases of SEQ ID NO:1. Evans et al. meet these limitations (Sequence Comparison B; columns 18-19).

10. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 27 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. in view of Xie et al. The claims recite methods of screening compounds for opioid binding activity using chimeric opioid receptors. The teachings of Evans are seen above. Evans et al. do not teach opioid chimeras. However, Xie do teach opioid chimeras. It would have been obvious to one of ordinary skill in

the art at the time of the present invention to have made an opioid chimera using the opioid of Evans in the method of Xie in order to further characterize the binding and functional characteristics of the protein of Evans. There would have been a reasonable expectation of success in using the protein of Evans in the method of Xie since recombinant techniques were well-known and highly successful in the art at the time of the present invention.

A. Claims 27 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. in view of Xie et al. for the reasons taught in paragraph A in this rejection. The teachings of Chen are seen in paragraph A of the rejection under 35 USC 102.

11. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
October 17, 2003

ROBERT LANDSMAN
PATENT EXAMINER